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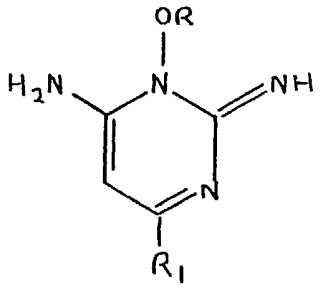
None

(58) Field of search
C2C

(54) Pyrimidine compounds for the growth of hair and cosmetic formulations containing such compounds

(57) New salts of general formula I:



· A (I)

in which R represents hydrogen or an $SO_3^{(-)}$ group; R_1 represents a piperidin-1-yl, 3-hydroxypiperidin-1-yl, 4-hyroxypipidin-1-yl or 4-carboxybutylamino grouping, with the condition that, when R is hydrogen, R_1 is not piperidin-1-yl; when R is hydrogen A represents a compound of acid nature, selected from the group which comprises N-acetyl cysteine, thiosalicylic acid, S-carboxymethyl cysteine and 2-benzoymercapto-propionylglycine; when R is an $-SO_3^{(-)}$ group, A represents, on the contrary, a compound of basic nature, selected from the group which comprises arginine, methyl cysteine, lysine or the dimethyl ester of the carboxy-cysteine; and groups A derived from amino acids may be in the L, D or D, L form, are useful as activators for the growth of hair and for the treatment of different forms of alopecia.

Processes for the preparation of the free pyrimidines (I) are also claimed.

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SPECIFICATION

Compounds for the growth of hair and cosmetic formulations containing such compounds

The present invention relates to novel salts useful as activators for the growth of hair, a process for the preparation of the said salts and the formulations which contain them as active ingredients.

Products are already known which have been proposed for the treatment of changes of the scalp, these having an influence on the aesthetics of the person. Even if they have a doubtful result as regards the conservation of the head of hair, these products provide advantages in counteracting alopecia, baldness and seborrheic conditions, when they are employed at the time of the commencement of the pathological manifestations.

The formulations of such products are compounded with a hydro-alcoholic-glyceric medium which is balanced so as to favour the activity of the active ingredients, formed by active ingredients such as camphor, thymol, colloidal sulphur, resorcin, quinine salts, pilocarpine, acetyl resorcin, bactericides, fungicides and microergics (Vitamin A, Vitamin B_6, pantothenic acid, oestrogens, placentary extracts, heparinoids).

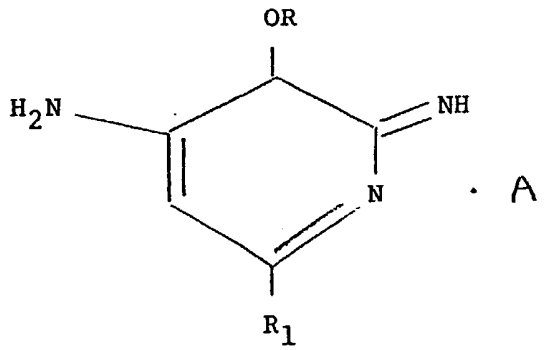
In the cosmetic filed, there are also used other products capable of intervening in respect of damage to the hair follicle due to aesthetic treatments (permanent waving, bleaching, dyeing) or related to constitutional or ambient factors.

These products, of which the efficacy has been insufficiently documented, comprise first of all the proteic lysates of prolamines and scleroproteins (horny material, hair, feathers, collagen, horsehair) which, on account of the affinity for the elements of cornea production, act by forming a compensatory thin layer, capable of repairing mechanically the processes of wear. From a therapeutic point of view, the existing formulations have to be considered as means which have a simply symptomatic signification or a generally preventive effect.

A topical or local effect on the scalp has recently been shown in the case of a known medicament with a cradio-vascular effect, this being Minoxidyl or 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-piperidinopyrimidine (U.S. Patent No. 3382247).

The present invention is concerned with salts of the general formula I:

(I)



in which R represent hydrogen or an $SO_3^{(-)}$ group; R_1 represents a piperidin-1-yl, 3-hydroxypiperidin-1-yl, 4-hydroxypiperidin-1-yl or 4-carboxybutylamino group, with the condition that, when R is hydrogen, R_1 is not piperidin-1-yl;

When R is hydrogen A represents a compound of acidic nature, selected from the group which comprises N-acetylcysteine, thiosalicyclic acid, S-carboxy-cysteine and 2-benzoylmercapto-propionylglycine; when R is an $-SO_3^{(-)}$ group, A represents, on the contrary, a compound of basic nature which is selected from the group which comprises arginine, methyl cysteine, lysine or the dimethyl ester of carboxy-cysteine; and A groups derived from amino acids may be in the L, D or D,L form.

Compounds I have shown a stimulating activity for the growth of hair.

The components having a pyrimidinic structure in the salts forming the subject of the present invention, i.e. 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(3-piperidinol) pyrimidine, 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-piperidinol) pyrimidine, 6-amino-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine and 2,6-diamino-4-(1-piperidinyl)-1-(sulphoxy) pyrimidine, are the metabolites of Minoxidyl and are deprived of activity on the vascular system, with the exception of the 2,6-diamino-4-(1-piperidinyl)-1-(sulphoxy) pyrimidine.

It has now surprisingly been found that all the metabolites retain the same activity on the hair as that of Minoxidyl and that the novel salts of the metabolites forming the subject of the present invention show an action superior to that given by Minoxidyl by itself, in equivalent quantities, in the same cosmetic formulations.

As a consequence of prolonged daily use, for 2 to 3 months, we have found that the cosmetic formulations of the invention make it possible to obtain satisfactory responses in the treatment of different forms of alopecia and in the control of the functional states of "scaling" of the hair structures which cause the progressive process of the balding.

The novel salts which are the subject of the invention are conveniently added, in proportions between 0.2 and 10%, to balms, shampoos, creams and lotions, either individually, or mixed or combined with other active substances. As well as cosmetic formulations, the invention also seeks to provide processes for obtaining each

compound and its novel salts.

The inactive metabolites may be obtained by reaction of 4-chloro-2,6-diaminopyrimidine with 3- or 4-hydroxy-piperidine or 5-aminopentanoic acid in excess, followed by an oxidation with hydrogen peroxide in a methanolic solution, this giving the corresponding N-oxides which, by being heated at 60°, are transformed into the desired hydroxy derivatives.

The sulphonated active metabolite ($R = SO_3^-$, R_1 = 1-piperidinyl) is obtained by the reaction of the Minoxidyl in pyridine with chlorosulphonic acid at a temperature not above 5°. By distillation of the pyridine, acidification and treatment with acetonitrile, there is obtained the sulphoxy derivative.

According to the present invention, the salts of the non-vasoactive metabolites are prepared by reaction with N-acetyl cysteine, thiosalicic acid, S-carboxymethyl cysteine, or N-(2-benzoyl thiopropionyl) glycine in a molar ratio of 1:1 in a solution or suspension in solvents which are preferably formed by the C_1-C_4 alcohols, possible containing water in smaller proportions, at a temperature between 10°C and 100°C, preferably the boiling temperature of the solvent. The desired salts are obtained by cooling the solution or by evaporating the solvent. The salts may be obtained by adding acetone to the cooled solution or by lyophilising the aqueous solutions which contain them.

The salts of the sulphonated vasoactive metabolite are prepared by causing it to react with methyl cysteine, arginine, lysine or dimethyl S-carboxycysteine in a molar ratio of 1:1 in a solution or suspension in solvents which are preferably constituted by C_1-C_4 alcohols, possible containing water in smaller proportions, at a temperature which is between 10° and 100°, preferably the boiling temperature of the solvent. The desired salts are obtained by cooling the solutions as thus obtained or by evaporating the solvent.

The salts may also be obtained by adding acetone to the cooled solution or by lyophilising the aqueous solutions which contain them.

The Examples which follow hereafter illustrate the invention, without limiting it in any way.

EXAMPLE 1

(a) *2,6-diamino-4-(3-hydroxypiperidin-1-yl) pyrimidine*

3 g. of 4-chloro-2,6-diaminopyrimidine are heated at 100° for 1½ hours with 30 g. of 3-hydroxypiperidine, re-cooled and filtered. The solid is mixed with vigorous stirring with 30 ml of NaOH alkaline solution.

Filtration is carried out, followed by extraction with boiling acetonitrile. After cooling and filtration, about 3.2 g. of the desired product are obtained. The structure is confirmed by elementary analyses.

Elementary analysis (M.W. = 209.25)

	C	*H*	*N*
Calculated (%)	51.66	7.23	33.47
Found (%)	51.71	7.30	33.43

(b) *6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(3-hydroxypiperidin-1-yl) pyrimidine*

30 ml of hydrogen peroxide (30%) are added to a solution of 18 g. of the compound prepared in (a) in 100 ml of methanol; the stirring is maintained for 1 hour, the solvent is evaporated and the residue is heated at 60° for 30 minutes. The latter is cooled and cystallised in absolute ethanol. 15 g. of the desired product are obtained. The structure is confirmed by spectral analyses.

Elementary analysis (M.W. = 225.25)

	C	*H*	*N*
Calculated (%)	47.99	6.71	31.09
Found (%)	48.01	6.74	31.05

Examples 2-3

Using the operating procedure of Example 1, but replacing the 3-hydroxypiperidine by 4-hydroxypiperidine and 5-aminopenatnoic acid, there are obtained the products which are set out in the following Table.

TABLE

Compound	*Yield in g.*	*Mol. weight*	*ELEMENTARY ANALYSIS calc. found*		
			C	*H*	*N*
6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-hydroxypiperidin-1-yl) pyrimidine	15	225.25	47.99% 48.110%	6.71% 6.81%	31.09% 31.05%
6amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino)-pyrimidine	15.5	242.26	44.62% 44.70%	6.66% 6.72%	28.91% 28.94%

EXAMPLE 4

2,6-diamino-4-(1-piperidinyl)-1-(sulphoxy)pyrimidine hydroxide

29.09 g. of 6-amino-1,2-dihydro-1-1hydroxy-2-imino-piperidino-pyrimidine are dissolved in 100 ml of pyridine. The solution is cooled to 0° and, while keeping the temperature at 0°C and while stirring, 12 g. of chlorosulphonic acid are slowly added. The stirring is maintained for 1 hour at 0°, 100 ml. of water are added and the solution is distilled *in vacuo* to a reduced volume. The residue is dissolved in 50 ml of water, which contains 2% of sodium carbonate, extraction with chloroform is carried out, the aqueous solution is acidified and then it is concentrated.

Crystallisation is allowed to take place at 10°, thereby obtaining 23 g. of product. The special analyses confirm the structure.

Elementary analysis (M.W. = 289.3)

	C	*H*	*N*	*S*
Calculated (%)	37.36	5.23	24.21	11.08
Found (%)	37.51	5.32	24.36	11.05

EXAMPLE 5

N-acetyl cysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4 (3-hydroxypiperidin-1-yl) pyrimidine (SKM/014)

21.69 g. of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(3-hydroxypiperidin-1-yl) pyrimidine and 16.32 g. of N-acetyl cysteine are dissolved under heat in 100 ml of isopropyl alcohol. The solution is cooled, 300 ml of acetone are added and the formed precipitate is separated, this being washed with acetone and dried in an oven.

About 35 g. of product are obtained. The structure is confirmed by spectral analyses.

Elementary analysis (M.W. = 388.44)

	C	*H*	*N*	*S*
Calculated (%)	43.29	6.23	21.64	8.25
Found (%)	43.40	6.24	26.71	8.20

Examples 6-8

Operating as described in Example 5, but employing appropriate reactants instead of the N-acetyl cysteine, there are obtained the salts of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(3-hydroxypiperidin-1-yl) pyrimidine, which are set out in the following Table.

TABLE

Reactant used	*Yield in g.*	*Mol. weight*	*ELEMENTARY ANALYSIS*			*calc. found*
			C	*H*	*N*	*S*
Thiosalicylic acid (SKN/015)	35	379.45	60.65% 61.56%	5.58% 5.60%	18.46% 18.41%	8.45% 8.48%
S-carboxymethyl cysteine (SKM/016)	37	404.44	41.58% 41.61%	5.98% 5.99%	20.78% 20.78%	7.93% 7.99%
2-benzoyl mercaptopropionyl glycine (SKM/017)	46	492.55%	51.21% 51.30%	5.73% 5.81%	17.05% 17.10%	6.51% 6.53%

EXAMPLE 9

N-acetyl cysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4(4-hydroxypiperidin-1-yl) pyrimidine, SKM/018

21.69 g. of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-hydroxypiperidin-1-yl) pyrimidine and 16.32 g. of N-acetyl cysteine are dissolved under heat in 100 ml of isopropyl alcohol. The solution is colled, 300 ml of acetone are added and the formed precipitate is separated, this being washed with acetone and dried in an oven. About 35 g. of product are obtained. The structure is confirmed by spectral analyses.

Elementary analysis (M.W. = 388.44)

	C	*H*	*N*	*S*
Calculated (%)	43.29	6.23	21.64	0.25
Found (%)	43.41	6.36	20.90	0.27

Examples 10-12

Using the operating procedure of Example 9, but replacing the N-acetyl cysteine by appropriate reactants, there are obtained the salts of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-hydroxypiperidin-1-yl) pyrimidine,

which are grouped in the following Table.

TABLE

Reactant used	*Yield in g.*	*Mol. weight*	*ELEMENTARY ANALYSIS*			*calc. found*
			C	*H*	*N*	*S*
Thiosalicylic acid (SKM/019)	35	379.45	50.65% 51.19%	5.58% 5.61%	18.46% 18.41%	8.45% 8.42%
S-carboxymethyl cysteine (SKM/020)	39	404.44	41.58% 41.62%	5.98% 6.00%	20.78% 20.71%	7.93% 7.91%
2-benzoyl mercaptopropionyl glycine (SKM/021)	46.5	492.55%	51.21% 51.31%	5.73% 5.83%	17.05% 17.10%	6.51% 6.53%

EXAMPLE 13

N-acetylcysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine (SKM/022)

23.29 g. of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine and 16.32 g. of acetyl cysteine are dissolved under heat in 80 ml of ethyl alcohol at 95° c.s. The solution thus obtained is concentrated in vacuo to about 30 ml; by cold crystallisation, about 37 g. of the desired salt are obtained. The structure is confirmed by spectral analyses.

Elementary analysis (M.W. = 390.44)

	C	*H*	*N*	*S*
Calculated (%)	43.07	6.20	17.94	8.21
Found (%)	43.12	6.18	18.05	8.28

Examples 14-16

Using the operating procedure of Example 3, but replacing the N-acetyl cysteine by appropriate reactants, there are obtained the salts of 6-amino-1,2-dihydro-1-hydroxy-4-(4-carboxybutylamino) pyrimidine grouped in the following Table.

TABLE

Reactant used	*Yield in g.*	*Mol. weight*	*ELEMENTARY ANALYSIS*			*calc. found*
			C	*H*	*N*	*S*
Thiosalicylic acid (SKM/023)	36	382.45	50.25% 51.16%	5.80% 5.81%	14.65% 14.63%	8.38% 8.31%
S-carboxymethyl cysteine (SKM/024)	37	406.44	8.41% 8.45%	5.95% 6.01%	17.23% 17.28%	7.8% 7.8%
2-benzoyl mercaptopropionyl glycine (SKM/025)	46	494.55%	51.0% 51.2%	5.71% 5.80%	14.16% 14.18%	6.48% 6.41%

EXAMPLE 17

2,4-diamino-4-(1-piperidinyl)-1-(methylcysteine sulphoxylate) pyrimidine (SKM/026)

19.9 g. of methyl cysteine are added to a solution of 28.19 g. of 2,6-diamino-4-(1-piperidinyl)-1-(sulphoxy)-pyrimidine hydroxide in 100 ml of water. After solubilization, the solution is lyophilised. 40.09 g. of the desired product are obtained. The structure is confirmed by spectral analyses.

Elementary analysis (M.W. = 422.5)

	C	*H*	*N*	*S*
Calculated (%)	39.80	5.73	16.58	15.18
Found (%)	39.85	5.86	16.71	15.08

Examples 18-20

Using the operating procedure of Example 17, but replacing the methyl cysteine by appropriate reactants, there are obtained the salts of the 2,6-diamino-4-(1-piperidinyl)-1-(sulphoxy)pyrimidine which are included in the following Table.

TABLE

Reactant used	*Yield in g.*	*Mol. weight*	*ELEMENTARY ANALYSIS*			*calc. found*
			C	*H*	*N*	*S*
Arginine (SKM/027)	44.8	449.52	40.08% 40.01%	6.50% 6.52%	24.93% 24.96%	7.13% 7.17%
Lysine (SKM/028)	41.55	416.48	43.26% 43.31%	5.81% 5.90%	20.18% 20.15%	7.70% 7.65%
Dimethyl carboxycysteine (SKM/029)	48.1	482.56	39.83% 39.88%	5.85% 5.91%	14.51% 14.59%	13.29% 13.21%

EXAMPLES OF FORMULATATIONS

Example A – Shampoo

Sodium lauryl ethoxylate (27%)	600 g
Coconut diethanolamide (90%)	60 g
Ethylene glycol monostearate	20 g
Stearic diester of polyethylene glycol	20 g
Colour	2.5 g
Perfume	5 g
Preservative	q.s.
SMK/020-SKM/021-SKM/022	ana 2.0 g
Deionised water	q.s.f. 1000

Example B – Shampoo

Sodium lauryl ethoxylate (27%)	600 g
Coconut diethanolamide (90%)	60 g
Ethylene glycol monostearate	20 g
Stearic diester of polyethylene glycol	20 g
Colour	2.5 g
Preservative	q.s.
SKM/014-SKM/016-SKM/017-SKM/018-SKM/019	ana 2.0 g
Deionised water	q.s.f. 1000

Example C – Lotion

Isopropyl myristate	10 g
PEG 6000 DS	20 g
Cetyl alcohol	20 g
Antioxidant	1.0 g
Carbopol 940	1.5 g
10% sodium hydroxide solution	3 ml
EDTA	0.5 g
Ethanol	30 ml
Perfumed composition	5 g
SKM/015	10 g
Deionised water	q.s.f. 1000

Example D – Lotion

Isopropyl myristate	10 g
PEG 6000 DS	20 g
Cetyl alcohol	20 g
Antioxidant	1.0 g
Carbopol 940	1.5 g
10% sodium hydroxide solution	3.0 ml
EDTA	0.5 g
Ethanol	30 ml
Perfumed composition	5 g
SKM/015-SKM/0167-SKM/020	ana 0.335 g
Deionised water	q.s.f. 1000

Example E – Lotion

Isopropyl myristate		10 g
PEG 6000 DS		20 g
Cetyl alcohol		20 g
Antioxidant		1.0 g
Carbopol 940		1.5 g
10% sodium hydroxide solution		3.0 ml
EDTA		0.5 g
Ethanol		30 ml
SKM/014-SKM/015-SKM/016		
SKM/017-SKM/018-SKM/109-SKM/020	ana	0.56 g
Deionised water	q.s.f.	1000

Example F – Balm

Cetyl alcohol		25 g
Solulan		10 g
Quarternary ammonium		10 g
Nesatol		10 g
Silicones		5 g
Monopropylene glycol		10 g
Glicam P 10		10 g
PEG 6000 DS		30 g
Preserving mixture		5 g
Perfume		4 g
SKM/022-SKM/023-SKM/024-SKM/025	ana	2.5 g

Example G – Ointment

Cetomacrogal		18 g
Cetyl stearic alcohol		240 g
Solid paraffin		150 g
Liquid paraffin		60 g
Perfume		q.s.
Preservative		q.s.
Monosodium and bisodium phosphate q.s. for pH		6.0
SKM/026-SKM/027-SKM/028-SKM/029	ana	1.0 g
Deionised water	q.s.f.	1000

The novel salts according to the invention are provided with biological activities which activate the functions of the follicles, which are transformed into the prolongation of the "anagen" phase during the growth of the hair.

Local application of the compounds according to the present invention causes an acceleration of the growth of the hair or fur in rodents having alopecia induced by a chronic treatment with thallium slats. After suspension of the toxic treatment, the growth of the new fur in the zones which were attacked is found to be much faster as compared with that observed in the animals treated locally with other products in current use or in animals treated locally with equivalent quantities of Minoxidyl.

Another surprising observation concerns the effect which is shown by the salts of non-vasoactive metabolities, of which the activity, from a quantitive point of view, is shown to be more intense than that of the same Minoxidyl applied locally in equivalent quantities.

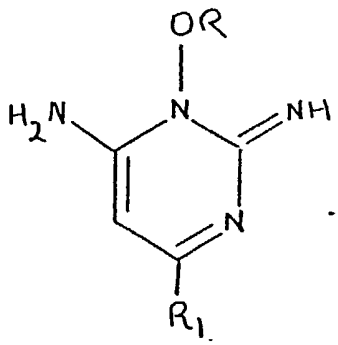
Experiments carried out on New Zealand rabbits or Bourgogne rabbits have demonstrated that the local application of the compounds according to the invention determines a consistent improvement in the speed of growth of the hair or fur in previously shaved cutaneous zones and in addition decreases the entity of the spontaneous depilation in the intact cutaneous zones. In the treated zones, previously subjected to shaving, the average speed of growth of the hair or fur is shown to be 0.3 mm/die, this being about 35% greater than that found in the untreated zones.

These observations were made with a sample of 80 rabbits. The maximum activity was observed after 45-60 days of treatment with 1 mg/die of each salt in two applications per day.

The aforementioned experiments have confirmed the surprising efficacy in the local treatment with the salts of non-vasoactive metabolities, which is greater than that which was shown when employing equivalent quantities of Minoxidyl.

CLAIMS

1. Compounds of general formula I

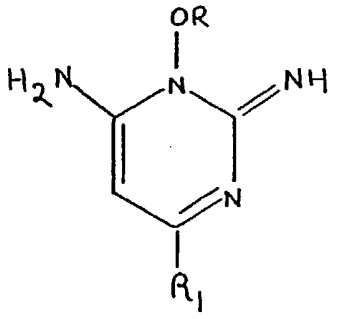


. A (I)

in which
R represents hydrogen or an $SO_3^{(-)}$ group;
R_1 represents a piperidin-1-yl, 3-hydroxypiperidin-1-yl, 4-hydroxypipidin-1-yl or 4-carboxybutylamino grouping, with the condition that, when R is hydrogen, R_1 is not piperidin-1-yl;
when R is hydrogen A represents a compound of acid nature, selected from the group which comprises N-acetyl cysteine, thiosalicyclic acid, S-carboxymethyl cysteine and 2-benzoylmercapto-propionylglycine; when R is an $-SO_3^{(-)}$ group, A represents, on the contrary, a compound of basic nature, selected from the group which comprises arginine, methyl cysteine, lysine or the dimethyl ester of the carboxy-cysteine; and groups A derived from amino acids may be in the L, D or D,L form.

2. Compound according to claim 1, selected from the group constituted by:
– N-acetylcysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(3-hydroxypiperidin-1-yl) pyrimidine;
– thiosalicylate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4(3-hydroxypiperidin-1-yl) pyrimidine;
– S-carboxymethylcysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(3-hydroxypiperidin-1-yl) pyrimidine;
– 2-benzoylmercaptopropionyl glycinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-hydroxypiperidin-1-yl) pyrimidine;
– N-acetyl cysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine;
– thiosalicylate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine;
– S-carboxymethyl cysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine;
– 2-benzoylmercaptopropionyl glycinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-hydroxypiperidin-1-yl) pyrimidine;
– N-acetyl cysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine;
– Thiosalicylate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine;
– S-carboxymethyl cysteinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine;
– 2-benzoylmercaptopropionyl glycinate of 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-(4-carboxybutylamino) pyrimidine;
– 2,6-diamino-4-(1-piperidinyl)-1-(methyl cysteine sulphoxylate)-pyrimidine;
– 2,6-diamino-4-(1-piperidinyl)-1-(arginine sulphoxylate)-pyrimidine;
– 2,6-diamino-4-(1-piperidinyl)-1-(lysine sulphoxylate)-pyrimidine;
– 2,6-diamino-4-(1-piperidinyl)-1-(dimethylcarboxy cysteine sulphoxylate)-pyrimidine.

3. Process for the preparation of the compounds of formula I, comprising reacting the compounds of formula:

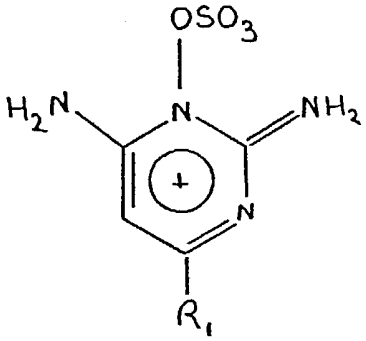


(Ia)

in which R and R_1 have the meanings specified above, with the compounds A, in almost stoichiometric quantities in solution or in suspension in water C_1-C_4 alcoholic solvents at the boiling temperature of the solvent, and isolating the salt I by crystallisation in the partially or entirely evaporated solvent, with addition of acetone, or by lyophilisation when the solvent is water.

4. Process for the preparation of the compounds of formula (Ia), where R and R_1 have the meanings specified above, comprising reacting 2,6-diamino-4-chloropyrimidine at about 100° in pyridine with an excess of 3- or 4-hydroxypiperidine or 5-aminopentanoic acid and oxidising the product thus obtained by hydrogen peroxide in a methanolic solution and then heating for half an hour at 60°C.

5. Process for the preparation of the compounds of formula (Ib)



(Ib)

in which R_1 represents piperidin-1-yl, comprising reacting 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-piperidino-pyrimidine with chlorosulphonic acid in pyridine.

6. Cosmetic compositions for the growth of hair and for the treatment of alopecias, containing as active ingredient, one or more compounds according to claim 1 or 2.

7. Cosmetic compositions according to claim 6, in the form of shampoos, lotions, balms, ointments or creams.

8. Compositions according to claim 6 or 7, wherein the active ingredients are present in percentages which are between 1 and 10%.

9. A compound according to claim 1 substantially as described herein and exemplified.

10. A process for the preparation of compounds of formula I substantially as described herein and exemplified.

11. A cosmetic composition according to claim 6 substantially as described herein and exemplified.

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